WO 2004/009056 PCT/EP2003/008005

- 22 -

<u>Claims</u>

- 1. Semisolid ophthalmic composition, in particular ointment, comprising
 - (1) an ophthalmic drug,
 - (2) an ointment base and
 - (3) an agent for dispersing and/or dissolving said drug in the ointment base, selected from a poly(ethylene-glycol), a polyethoxylated castor oil, an alcohol having 12 to 20 carbon atoms and a mixture of two or more of said components.
- 2. Composition according to claim 1, wherein the ointment base comprises
 - (a) a natural wax, preferably a white or yellow bees wax, a carnauba wax, a wool wax (wool fat), a purified lanolin or an anhydrous lanolin,
 - (b) a petroleum wax, preferably a hard paraffin or a microcrystalline wax,
 - (c) a hydrocarbon, preferably a liquid paraffin, a white or yellow soft paraffin or a white petrolatum or yellow petrolatum, or
 - (d) a combination of two or more of such components.
- 3. Composition according to claim 2, wherein the ointment base comprises a combination of
 - (a) one or more natural waxes, preferably a wool wax (wool fat), and
 - (c) one or more hydrocarbons, preferably a soft paraffin or a petrolatum, more preferably in combination with a liquid paraffin.
- 4. Composition according to claim 3, wherein the ointment base comprises
 - (a) 5 to 17 parts by weight of wool fat, and
 - (c1) 50 to 65 parts by weight of white petrolatum, and
 - (c2) 20 to 35 parts by weight of liquid paraffin.
- 5. Composition according to claim 1, wherein the agent for dispersing and/or dissolving the drug in the ointment base is selected from a poly(ethylene-glycol), a polyethoxylated castor oil and a mixture of said components.

- 6. Composition according to claim 5, wherein the agent for dispersing and/or dissolving the drug in the ointment base is a mixture of a poly(ethylene-glycol) and a polyethoxylated castor oil.
- 7. Composition according to claim 5 or 6, wherein the poly(ethylene-glycol) has the formula H-(OCH₂-CH₂)_nOH, wherein n is a number from about 6 to about 22.
- 8. Composition according to claim 5 or 6, wherein n is a number from about 6 to about 13.
- 9. Composition according to claim 5 or 6, wherein n is a number from about 8.5 to about 9.
- 10. Composition according to claim 5 or 6, wherein the polyethoxylated castor oil has a molecular weight (by steam osmometry) of about 1630, a saponification no. from about 65 to about 70, an acid no. of about 2, an iodine no. from 28 to about 32 and a n_D²⁵ of about 1.471.
- 11. Composition according to claim 5 or 6, wherein the polyethoxylated castor oil is Cremophor®EL.
- 12. Composition according to claim 1, wherein the agent for dispersing and/or dissolving the ophthalmic drug in the ointment base is used in amounts of 1 to 20 percent by weight of said composition.

5

- 13. Composition according to claim 1, wherein the ophthalmic drug is selected from
 - a COX-2 inhibitor of the following formula

WO 2004/009056 PCT/EP2003/008005

- 24 -

$$\begin{array}{c|c} R & CH_2COOH \\ \hline & NH \\ R_1 & R_5 \\ \hline & R_2 & R_4 \end{array}$$

wherein

R is methyl or ethyl;

R₁ is chloro or fluoro;

R₂ is hydrogen or fluoro;

R₃ is hydrogen, fluoro, chloro, methyl, ethyl, methoxy, ethoxy or hydroxy;

R₄ is hydrogen or fluoro; and

R₅ is chloro, fluoro, trifluoromethyl or methyl, preferably 5-methyl-2-(2'-chloro-6'-fluoroanilino)phenyl acetic acid, an ophthalmically acceptable salt thereof; or an ophthalmically acceptable prodrug ester thereof;

a compound of the following formula

$$N = X (CHR)_n Y$$

wherein

n is 0 to 2,

R is H or lower alkyl;

X is imino, oxa, or thia;

Y is aryl; and

Z is unsubstituted or substituted pyridyl,

or an N-oxide of the defined compound, wherein one or more N atoms carry an oxygen atom,

preferably 1-(3-Chloroanilino)-4-(4-pyridylmethyl)phthalazine, or an ophthalmically acceptable salt thereof; and particularly from

- an ascomycin;
- a staurosporine derivative, especially a staurosporine derivatives of formula (I)

wherein

R is a hydrocarbyl radical or an acyl radical, or an ophthalmically acceptable salt thereof.

- 14. Composition according to claim 13, wherein the ophthalmic drug is a staurosporine derivative of formula (I) and R is preferably benzoyl (also known as PKC 412 or CGP 41251).
- 15. Composition according to claim 1, further comprising a preservative, in particular selected from quaternary ammonium compounds, cetrimide and phenyl ethyl alcohol.
- 16. Composition according to claim 1, further comprising an antioxidant, in particular a natural or synthetic Vitamin E derivative, especially alpha-tocopherol or alpha-tocopherol acetate.
- 17. Composition according to claim 1 or 13, comprising or, preferably, consisting essentially of

 (1) an ophthalmic drug, in particular a staurosporine derivative of formula (I),

- (2) an ointment base, preferably comprising a combination of
 - (a) one or more natural waxes, preferably a wool wax (wool fat), and
 - (b) one or more hydrocarbons, preferably a soft paraffin or a petrolatum, more preferably in combination with a liquid paraffin,
- (3) an agent for dispersing and/or dissolving the drug in the ointment base selected from a poly(ethylene-glycol) and a mixture of a poly(ethylene-glycol) and a polyethoxylated castor oil, and optionally
- (4) a preservative, in particular phenyl ethyl alcohol and, optionally too,
- (5) an antioxidant, in particular a natural or synthetic Vitamin E derivative.
- 18. Composition according to claim 13 comprising or, preferably, essentially consisting of
 - 0.1 to 4, preferably 0.4 to 1.5 percent of a staurosporine derivative of formula (I), more particular PKC 412;
 - (2) an ointment base, essentially consisting of a combination of
 - (a) 5 to 17 percent of wool fat,
 - (c1) 50 to 65 percent of white petrolatum and
 - (c2) 20 to 35 percent of liquid paraffin;
 - (3) 1 to 10 percent of an agent for dispersing and/or dissolving the drug in the ointment base essentially consisting of a poly(ethylene-glycol), optionally in combination with a polyethoxylated castor oil, and
 - (4) 0.01 to 2 percent of a preservative, in particular phenyl ethyl alcohol as well as
 - (5) 0.01 to 2 percent of an antioxidant, in particular a natural or synthetic Vitamin E derivative,
 - wherein all percentages relate to the total weight of the components (1) to (5).
- 19. Composition according to claim 13 and comprising a staurosporine derivative for use in the treatment and/or prevention of human ocular neovascular diseases, more particularly in the treatment and/or prevention of human retinal and/or chorodial neovascular diseases, most preferably in the treatment and/or prevention of age-related macular degeneration (AMD), diabetic macular edema (DME), and/or proliferative diabetic retinopathy (PDR).

- 20. Method for the treatment and/or prevention of human ocular neovascular diseases, more particularly for the treatment and/or prevention of human retinal and/or chorodial neovascular diseases, most preferably for the treatment and/or prevention of age-related macular degeneration (AMD), diabetic macular edema (DME), and/or proliferative diabetic retinopathy (PDR), comprising topically administering a composition according to claim 13 and comprising a staurosporine derivative to the ocular surface, e.g. the sclera of a patient in need thereof.
- 21. Method according to claim 20 comprising the topical administration of the staurosporine derivative comprised in said semisolid composition to the ocular surface, in particular to the sclera of the patient, thereby targeting the choroid and/or retina in said patient.
- 22. Use of a composition according to claim 13 and comprising a staurosporine derivative, in the preparation of a medicament for the treatment and/or prevention of human ocular neovascular diseases, more particularly for the treatment and/or prevention of human retinal and/or chorodial neovascular diseases, most preferably for the treatment and/or prevention of age-related macular degeneration (AMD), diabetic macular edema (DME), and/or proliferative diabetic retinopathy (PDR).
- 23. Use according to claim 22, wherein the medicament is adapted to topical administration to the ocular surfaces of the eye, e.g. to the sclera, of a patient thereby targeting the choroid and/or retina in said patient.
- 24. Composition according to claim 13 and comprising an ascomycin for use in the treatment of inflammatory diseases, especially blepharitis e.g. chronic blepharitis, e.g. seborrhoeic blepharitis or allergic blepharitis.
- 25. Method for treating inflammatory diseases, especially blepharitis, e.g. chronic blepharitis, e.g. chronic blepharitis, e.g. seborrhoeic blepharitis or allergic blepharitis, comprising topically administering a

WO 2004/009056 PCT/EP2003/008005

- 28 -

composition according to claim 13 and comprising an ascomycin to the skin of a patient in need thereof.

- 26. Use of a composition according to claim 13 and comprising an ascomycin in the preparation of a medicament for the treatment of ocular inflammatory diseases, especially blepharitis e.g. chronic blepharitis, e.g. seborrhoeic blepharitis or allergic blepharitis.
- 27. Use according to claim 26, wherein said medicament is adapted to topical administration to the eye and/or its environment, e.g. to the skin of the eyelid or into the cul de sac of the eye or upon the ocular surfaces of the eye, of a patient in need thereof.